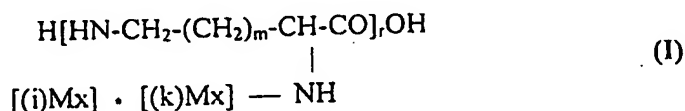


What we claim is:

1) Polycation bioconjugates characterized in that each of them contains isopolypeptide polycation carrier molecules having free α -amino groups, and these carrier molecules are conjugated by chemical bonds with suitably selected molecules which may either be identical ones or of (two or more i.e. "x") different kind, bearing functional groups appropriate for conjugation, and the polycation bioconjugates synthesized this way can be described by the general formula (I):



wherein:

"r" is a mean value between 20 and 400;

"m" = 0, 1, 2, 3, ... k;

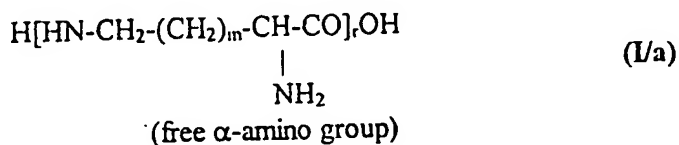
"[(k)Mx]" designates enhancer molecules and/or connecting molecules conjugated by covalent (= k) bonds to the isopolypeptide polycation carrier molecule, and

"[(i)Mx]" designates enhancer molecules conjugated by ionic (= i) bonds to the isopolypeptide polycation carrier molecule, whereas the said enhancer molecules and connecting molecules having appropriate functional groups for conjugation may either be identical ones or of (two or more i.e. "x") different kind, and the enhancer molecules can be conjugated:

- directly and/or
- indirectly through a connecting molecule,

and further the joint occurrence of [(k)Mx] and [(i)Mx] within the same polycation bioconjugate is symbolized by [(k/i)Mx].

2) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that in the consisting isopolypeptide polycation carrier molecules there are monomers of the same configuration (i.e. either D-, or L-), and the individual monomers are not linked together by their amino groups in the α -positions, but by those in other (i.e. in β -, γ -, δ -, ϵ -...etc.) positions - according to the value of "m", and thus the isopolypeptide polycation carrier molecules (furtheron: carrier molecules), having free α -amino groups, are of general formula (I/a):



wherein

"r" and "m" have the same meaning as in general formula (I).

3) Carrier molecules of general formula (I/a), prepared according to Claim 2, characterized in that their structure is divergent from that of the polypeptides build up by customary α -amino-peptide bonds, generally occurring in mammal organisms, and due to

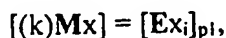
their divergent chemical structure, for instance the ϵ -amino-peptide bonds, they also exhibit divergent biological properties.

4) Carrier molecules of general formula (I/a), according to Claim 3, characterized in that they are more resistant to proteolytic enzymes, and thus are especially favourably applicable in transporting the active substances of different types within the mammal organism, i.e. for implementing carrier functions.

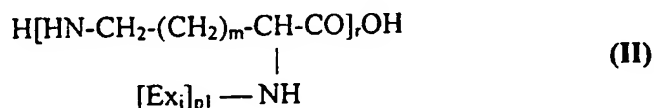
5) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that suitably selected [(k)Mx] and/or [(i)Mx] molecules, which may either be identical ones or of (two or more i.e. "x") different kind, are conjugated to a given representative of carrier molecules of general formula (I/a), by covalent and/or ionic bonds.

6) Polycation bioconjugates of general formula (I), according to Claim 5, characterized in that the conjugation of the [(k)Mx] and/or [(i)Mx] molecules to a given representative of carrier molecules of general formula (I/a), by covalent and/or ionic chemical bonds takes place directly and/or indirectly, in a definite ratio, preferably to reach a saturation of 10 to 100 %.

7) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that they include those bioconjugates in which a given representative of carrier molecules of general formula (I/a), is directly conjugated by covalent bonds with [Ex_i] enhancer molecules, which may either be identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates:



and the polycation bioconjugates are being described by the general formula (II):



wherein:

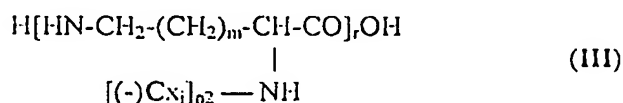
- "Ex" in [Ex_i]_{p₁} designates the Ex enhancer molecules of different ("x") kind conjugated directly to a given representative of carrier molecules of general formula (I/a), by covalent bonds, and
- "i" indicates whether the Ex enhancer molecules, conjugated to the given carrier molecule by covalent bonds, are identical ones (i = 1), or they are of different kind, of number "i" (i = 2, 3, ... "x" kind); and
- "p₁" indicates a degree of saturation in % of a carrier molecule of general formula (I/a) with [Ex_i] enhancer molecules, the value of which is > 0 and ≤ 100, whereby the ratio between the free (not involved in chemical bonds) and bound NH₂-groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates; and
- "r" and "m" have the same meaning as in general formula (I).

8) Carrier molecules of general formula (I/a), prepared according to Claim 2, characterized in that a given representative of them are conjugated by covalent bonds

with $[(-)Cx_j]$ connecting molecules of anionic character, which may either be identical ones or of (two or more i.e. "x") different kind, and the connecting molecules are suitably chosen dicarbonic acids, tricarbonic acids, carbohydrates, or amino acids, or peptide chain elongators, and in these compounds:

$$[(k)Mx] = [(-)Cx_j]_{p2}$$

and the conjugates are being described by the general formula (III):



wherein:

"(-)Cx" in $[(-)Cx_j]_{p2}$ designates (-)Cx connecting molecules of exclusively anionic character of different ("x") kind linked to a given representative of carrier molecules of general formula (I/a) by covalent bonds, and

"j" indicates whether the (-)Cx connecting molecules, conjugated to the given carrier molecule by molecule by covalent bonds, are identical ones ($i = 1$), or they are of different kind, of number "i" ($i = 2, 3, \dots$ "x" kind); and

"p₂" indicates a degree of saturation in % of a carrier molecule of general formula (I/a) by $[(-)Cx_j]$ connecting molecules of exclusively anionic character, the value of which is > 0 and ≤ 100 , whereby the ratio between the free (not involved in chemical bonds) and bound NH_2 - groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates; and

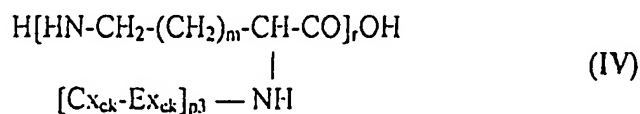
"r" and "m" have the same meaning as in general formula (I).

9) Conjugates of general formula (III), according to Claim 8, characterized in that the carrier molecules of general formula (I/a), of cationic character, due to conjugation of the $[(-)Cx_j]$ connecting molecules of anionic character to them by covalent bonds, become capable of building up such polycation bioconjugates, in which additional possibilities arise to establish ionic bonds with enhancer molecules of cationic character.

10) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which a given representative of carrier molecules of general formula (I/a) is indirectly conjugated with Ex enhancer molecules, which may either be identical ones or of (two or more i.e. "x") different kind, through Cx connecting molecules, which may also be either identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates both of the chemical bonds between the carrier molecule and Cx, as well as between the Cx and Ex, are covalent ones, and in these bioconjugates:

$$[(k)Mx] = [Cx_{ck}-Ex_{ck}]_{p3},$$

and the polycation bioconjugates are being described by the general formula (IV):

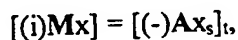


wherein:

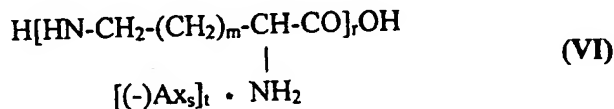
"[Ex]_i]_{p1}" has the same meaning as in general formula (II),
 "[(-)Cx]_j]_{p2}" has the same meaning as in general formula (III),
 "[Cx_{ck}-Ex_{ck}]_{p3}" has the same meaning as in general formula (IV),

"m" has the same meaning as in general formula (I), further the value of "p₁"+"p₂"+"p₃" > 0 and ≤ 100, and from among "p₁", "p₂" and "p₃" the value of at least two are greater than 0; further in a given polycation bioconjugate, the Ex molecules in [Ex]_i, and the (-)Cx molecules in [(-)Cx]_j are not necessarily identical with those Ex and Cx molecules occurring in [Cx_{ck}-Ex_{ck}] which divergence is symbolized by "x".

13) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which a given representative of carrier molecules of general formula (I/a) is directly conjugated, exclusively by ionic bonds with (-)Ax enhancer molecules of anionic character, which may either be identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates



and the polycation bioconjugates so obtained can be described by the general formula (VI):



wherein:

"(-)Ax" in [(-)Ax_s]_t designates those (-)Ax enhancer molecules of anionic character, which may either be identical ones or of (two or more i.e. "x") different kind, that are conjugated to a given representative of carrier molecules of general formula (I/a), by ionic bonds, and
 "s" indicates whether the anionic/polyanionic molecules, conjugated to the given polycation carrier molecule by ionic bonds, are identical ones (s=1), or, they are of different kind, of the number "s" (s = 2, 3, "x" kind); and
 "t" means a degree of saturation in % of the given representative of carrier molecules of general formula (I/a) by (-)Ax anions, the value of which is > 0 and ≤ 100, whereby the ratio between the free (not involved in chemical bonds) and bound NH₂-groups is determined, which in turn influences the charge and the cationic character of the polycation bioconjugates; and
 "r" and "m" have the same meaning as in general formula (I).

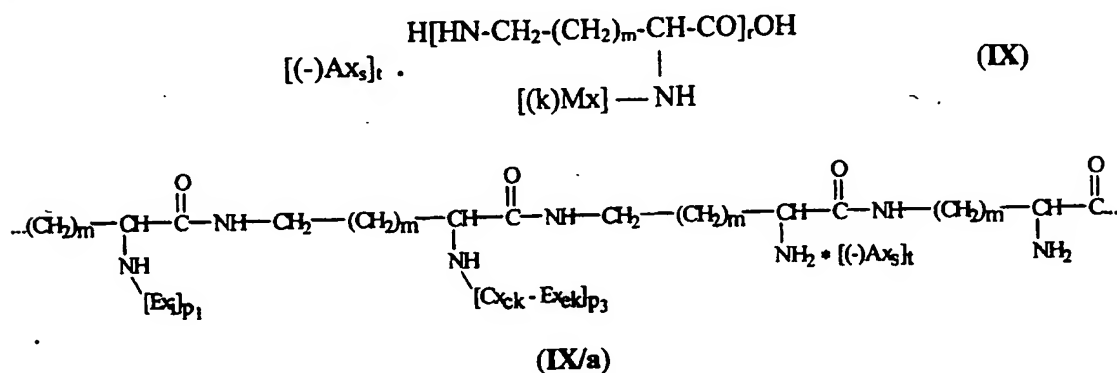
14) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include conjugates of general formula (III), prepared according to Claim 8, and these are conjugated with (+)Kx enhancer molecules of cationic character, which may either be identical ones or of (two or more i.e. "x") different kind, by ionic bonds via the (-)Cx connecting molecules of anionic character, and in these bioconjugates



16) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which to the free α -amino groups of a given representative of polycation bioconjugates of general formulae (II), (IV), or of schematic formula (V), prepared according to Claims 7, 10, and 12, as to a polycation, additional enhancer molecules which may either be identical ones (two or more i.e. "x") different kind, of anionic character $[(-)Ax_s]$ are conjugated by ionic bonds, and in these bioconjugates

$$[(k/i)Mx] = [Ex_i]_{p1} \cdot [(-)Ax_s]_t \text{ or } [Cx_{ck}-Ex_{ek}]_{p3} \cdot [(-)Ax_s]_t \text{ or } [Ex_i]_{p1} + [Cx_{ck}-Ex_{ek}]_{p3} \cdot [(-)Ax_s]_t,$$

and the polycation bioconjugates are being described by the general formula (IX), or by the schematic formula (IX/a):



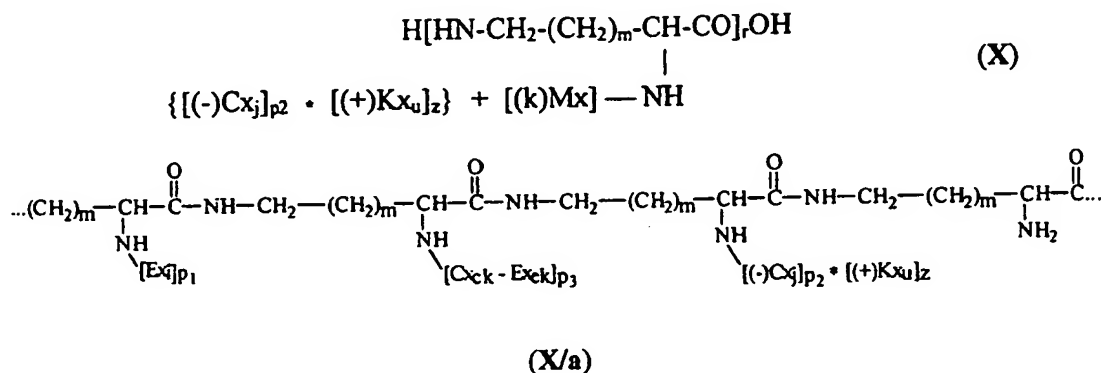
wherein:

"[(-)Ax _s] _t "	has the same meaning as in general formula (VI),
"[Ex _i] _{p1} "	has the same meaning as in general formula (II),
"[Cx _{ck} -Ex _{ek}] _{p3} "	has the same meaning as in general formula (IV),
"[(k)Mx]" and "m"	have the same meaning as in general formula (I), further
"p ₁ "+"p ₂ "+"t"	> 0 and ≤ 100, and from among
"p ₁ " and "p ₃ "	the value of at least one > 0; and
"t" > 0.	

17) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates which correspond to the polycation bioconjugates schematic formula (V), prepared according to Claim 12, including further those bioconjugates in which there are connecting molecules of anionic character $[(-)Cx_j]$ which may either be identical ones or of two or more "x" different kind, and these connecting molecules conjugate with ionic bonds the enhancer molecules of cationic character $[(+)Kx_u]$ which may either be identical ones or of (two or more i.e. "x") different kind, and in these bioconjugates

$$\begin{array}{l}
 [(k/i)Mx] = [Ex_i]_{p1} + \{ [(-)Cx_j]_{p2} \cdot [(+)Kx_u]_z \} \text{ or} \\
 [Cx_{ck}-Ex_{ek}]_{p3} + \{ [(-)Cx_j]_{p2} \cdot [(+)Kx_u]_z \}, \text{ or} \\
 [Ex_i]_{p1} + [Cx_{ck}-Ex_{ek}]_{p3} + \{ [(-)Cx_j]_{p2} \cdot [(+)Kx_u]_z \}
 \end{array}$$

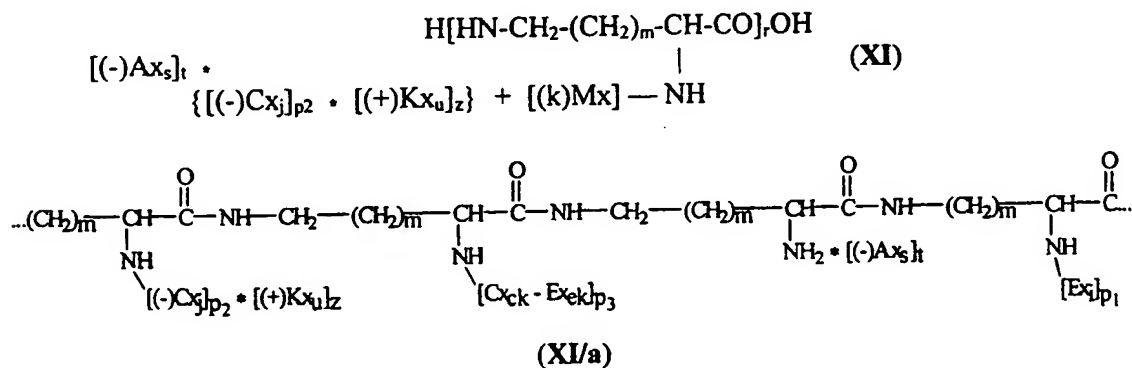
and the polycation bioconjugates are being described by the general formula (X), or by the schematic formula (X/a):



18) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they include those bioconjugates in which to the free α -amino groups of a given representative of polycation bioconjugates of general formula (X), or of schematic formula (X/a), prepared according to Claim 17, as to a polycation, additional enhancer molecules of anionic character $[(-)\text{Ax}_s]$ which may either be identical ones or of (two or more i.e. "x") different kind, are conjugated by ionic bonds, and in these bioconjugates

$$\begin{aligned}
 [(k/i)\text{Mx}] = & [\text{Ex}]_{p1} + \{[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z\} \cdot [(-)\text{Ax}_s]_t \text{ or} \\
 & [\text{C}_{\text{ck}} - \text{Ex}_{\text{ek}}]_{p3} + \{[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z\} \cdot [(-)\text{Ax}_s]_t \text{ or} \\
 & [\text{Ex}]_{p1} + [\text{C}_{\text{ck}} - \text{Ex}_{\text{ek}}]_{p3} + \{[(-)\text{Cx}_j]_{p2} \cdot [(+)\text{Kx}_u]_z\} \cdot [(-)\text{Ax}_s]_t,
 \end{aligned}$$

and the polycation bioconjugates are being described by the general formula (XI), or by the schematic formula (XI/a):



19) Carrier molecules of general formula (I/a), prepared according to Claim 2, having free α -amino groups, characterized in that they include hydrobromide salts of those 60 - 120 membered, non-racemic polyiso-L-lysines, i.e. poly-(ϵ)-L-lysine-hydrogen-bromides which themselves possess certain antitumor, antiproliferative and antiviral effect.

20) Carrier molecules of general formula (I/a), according to Claim 19, characterized in that they increase the antiproliferative or antiviral activities of the molecules linked to them.

21) Polycation bioconjugates, according to Claim 1, characterized in that in case the enhancer molecules conjugated to the suitably selected carrier molecule of general formula (I/a) themselves are not *ab ovo* possessing the wanted (eg. antiproliferative) activity, then as a consequence of their conjugation, they will boost the originally existing biological activity of the carrier molecule, for example of those prepared according to Claim 19.

22) Polycation bioconjugates of general formula (I), prepared according to Claim 1, characterized in that each of them contains carrier molecules of general formula (I/a) and these suitably selected carrier molecules are conjugated in a manner as shown on the general formulae (II), (III), (IV), (VI), (VII), (IX), (X), (XI), or on the schematic formulae (V), (VIII), (IX/a), (X/a), (XI/a), according to Claims 7, 8, 10, 12, 13, 14, 15, 16, 17 and 18, with practically any organic and/or inorganic molecule possessing functional groups appropriate for conjugation, and these latter may rationally be chosen - with a non-limiting manner - from among the groups of compounds, set out hereinbelow:

- hormones and hormone antagonists of different kind (steroid, protein, peptide, etc.), and active fragments of peptide hormones, and derivatives thereof;
- saturated and unsaturated fatty acids, cholesterol, phospholipids (phosphoglycerides, sphingomyelins, etc.), and derivatives thereof;
- nucleic acids/antisense nucleotides;
- monosaccharides, oligosaccharides, and polysaccharides, and derivatives thereof;
- vitamins, and their derivatives;
- known antitumor drugs and active substances, and derivatives thereof;
- amino acids, oligopeptides, polypeptides, further glycoproteins and lipoproteins, their fragments, and derivatives thereof.

23) Polycation bioconjugates of the general formula (I), according to Claim 1, characterized in that each of them contains carrier molecules of general formula (I/a), which are conjugated directly and/or indirectly, by covalent and/or ionic bond, with enhancer molecules having direct antiproliferative effect, which may either be identical ones or of (two or more i.e. "x") different kind, and these polycation bioconjugates are successfully applicable for treating malignant tumors occurring in mammal organisms, *in se*, or in combination with known antitumor methods, accepted in clinical practice.

24) Polycation bioconjugates of the general formula (I), according to Claim 23, characterized in that each of them contains carrier molecules of general formula (I/a), which are conjugated with additional enhancer molecules having indirect antiproliferative effect that is developing selectivity or increasing selectivity of bioconjugates towards a given target tumor cell, whereby they increase the concentration of the bioconjugates in the tumors, and thus the unwanted side-effects can be diminished, and the effectiveness of the treatment may further be increased.

25) Polycation bioconjugates of general formula (I), according to Claims 23 and 24, characterized in that in order to endow them with antitumor effect, a given representative of carrier molecules of general formula (I/a), is conjugated with compounds, suitably selected, from among the molecules having direct and/or indirect antiproliferative activity as demonstrated hereinbelow - by a non-limiting manner:

- compounds having direct antiproliferative effects: cytostatics used in the clinical practice, furthermore cytokines, which influence division and differentiation of tumor cells (eg.

different growth factors as well as antibodies produced against them, interferons, etc.), furthermore peptides/proteins inhibiting formation of new blood-vessels around the tumor cells (angiostatsins, endostatsins), further nucleic acids/antisense oligonucleotides which exert antiproliferative effects on the malignantly transformed cells;

- compounds of indirect antiproliferative effect, which develop selectivity or increase the selectivity of bioconjugates towards a given target cell: monoclonal antibodies having specific affinities to a surface antigen of a given tumor cell, as well as antibodies or any compound having affinity to those kind of receptors (for example transferrin receptor or folate receptor among the vitamins, etc.) which are present in a greater ratio on the surface of the tumor cells than of the normal (not malignantly transformed) cells;
- compounds having direct and simultaneously indirect antiproliferative effects: hormones, hormone antagonists and derivatives thereof, especially from among the polypeptide hormones the humane choriogonadotropine hormone, which having antiproliferative effects, furthermore antibodies produced against receptors of growth factors of different kind, which are present in greater ratio on the surface of a given tumor cell than on other cells, and simultaneously exert antiproliferative effects towards given malignantly transformed cells, furthermore immunotoxines, which are produced against a given tumor cell;

26) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that to a suitably selected given representative of the consisting carrier molecules of general formula (I/a), as to a polycation, a suitably selected nucleic acid - being a polyanion - is linked by ionic bond, and therefore the synthesized new conjugate is appropriate for gene transfer.

27) Polycation bioconjugates of general formula (I), according to Claim 26, characterized in that besides the nucleic acid coupled to the given representative of the consisting carrier molecules of general formula (I/a) by ionic bonds, additional molecules, which may either be identical ones or of two or more "x" different kind, capable of binding selectively and/or semi-selectively to target cells picked out for gene transfer, such as specific antibodies, hormones and molecules binding only to receptors on the surface of the target cells, which for example occur - due to non-pathological changes - exclusively on some cell types, namely to asialoglycoprotein receptor on liver cells (to which galactose residues in terminal position on the macromolecules are specifically binding to) or those molecules which are binding to receptors that occur more frequently (in more %) on the given target cells, are conjugated by covalent and/or ionic bonds, whereby a targeted gene transfer on cellular level is accomplished by the new conjugates.

28) Polycation bioconjugates of general formula (I), according to Claim 26 and Claim 27, characterized in that the bioconjugates, that are appropriate for gene transfer, consisting suitably selected isolated or synthesized nucleic acids, complexed antisense oligonucleotides, exhibit antiproliferative, antimicrobial effect, whereby for example inhibition of virus replication can be achieved, further they are enabling the treatment of genetic diseases (eg. cystic fibrosis).

29) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that to suitably selected given representatives of consisting carrier molecules of general formula (I/a) (which themselves possess certain antiviral activity) compounds having antimicrobial effect, (eg. antiviral, antibacterial, antimycotic, anti-protozoic compounds used in clinical practice, further complex antisense nucleic acids inhibiting

replication of viruses, antibodies of neutralizing effect) are conjugated, whereby the antimicrobial effect of the conjugated molecules increases.

30) Polycation bioconjugates of general formula (I), according to Claim 29, characterized in that besides the compounds of antimicrobial activity, conjugated to a given representative of carrier molecules of general formula (I/a), additional molecules, which may either be identical ones or of two or more "x" different kind, capable of binding selectively to microbes, such as specific antibodies that link to them, are conjugated, whereby the antimicrobial effect is further increasing.

31) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that to a given representative of consisting carrier molecules of general formula (I/a), paramagnetic contrast material, for example complex derivatives of gadolinium, is conjugated by means of chemical bonds, whereby the diagnostic value of nuclear magnetic resonance (NMR) imaging improves as compared to that of non-conjugated paramagnetic contrast material.

32) Polycation bioconjugates of general formula (I), according to Claim 31, characterized in that besides the molecules of the paramagnetic contrast material, conjugated to a given representative of included carrier molecules of general formula (I/a), they also include further suitably selected molecules - which may either be identical ones or of two or more "x" different kind - also conjugated, which are capable of being selectively enriched in organs, tissues, or pathological changes (eg. tumors) to be investigated, and the increase of their relative concentration within the given target area improves the image quality, additionally.

33) Polycation bioconjugates of general formula (I), according to Claims 31 and 32, characterized in that the molecules enhancing selectivity, which are conjugated to a given representative of the carrier molecules of general formula (I/a), are comprising antibodies, binding specifically to the target area to be investigated by NMR, or depending on the nature of the target area, also lipophilic or hydrophilic substances.

34) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they are being introduced into the target organism on transdermal route via iontophoresis.

35) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that they are capable of being appropriately incorporated into liposomes.

36) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that the regulating effect of the immune response modifying molecules, for example of the lymphokines (interleukines, interferons, etc.), that are conjugated to a given representative of carrier molecules of the general formula (I/a), as a constituent of the above polycation bioconjugates, is coming more favourably to full display.

37) Polycation bioconjugates of general formula (I), according to Claim 1, characterized in that these are being formulated in pharmaceutically acceptable forms, and the pharmaceutical preparates so obtained, are applicable perorally, or parenterally, or transdermally, for systemic or topical use.